

present cases and the term "may" has been deleted from claim 12. The term "periodic" is well supported by the specification and the Examiner's attention is directed to line 18 of page 2 wherein it is stated that the animal can be treated periodically, preferably daily but it can also be treated with a single administration. The expression "long lasting delivery" has been deleted from claim 16 and in claim 19, the term "basifying agent" has been changed to "basic agent". Claim 20 has been cancelled particularly in view of the Examiner's restriction requirement.

Claims 1 to 19 were rejected under 35 USC 103 as being obvious over the FDA Register, Papich or WO96/31213 taken alone or in any combination. The Examiner states that Papich discloses anti-ulcer drugs including omeprazole to prevent ulcers in small animals. The WO '213 reference is cited to show compositions comprising proton pump inhibitors and recited dosages and that they can be used to treat ulcers in animals. The FDA summary is cited to show that omeprazole is used to prevent ulcers in horses.

Applicant respectfully traverses these grounds of rejection since the combination of the prior art does not suggest Applicant's invention to one skilled in the art. Applicant's

invention is directed to preventing ulcers prior to the occurrence of gastric ulcers. Although ulcers heal rapidly, healing slows after four weeks and by eight weeks, as many as 4 to 10% have a reoccurrence indicating a refractory ulcer. The gastro intestinal ulcer disease is a chronic disease and as such, tends to reoccur frequently. There is a 50 to 90% relapse within one year after healing regardless of which acid supressive was used to heal initially. This means that there is a significant percentage of gastric ulcers that do not fully heal and there is a significant number of patients that suffer relapse within a year.

Clearly, a patient that has suffered from a gastric ulcer is different from a patient that has not had an ulcer. The patient that has suffered a gastric ulcer will more than likely suffer a relapse and a significant number of patients that have suffered a gastric ulcer do not have full healing and this makes a dramatic distinction between preventing relapse in a patient that has had an ulcer and preventing gastric ulcers in a patient that has not suffered from an ulcer. Therefore, patients that have suffered from gastric ulcers are clearly different from a patient that has not.

That omeprazole or other active principals can be used to treat gastric ulcers, for example in horses, or other active

principals can be used to treat gastric ulcers for examples in horses was admitted in the background portion of the specification. Similarly, reoccurrence of gastric ulcers can be prevented was also stated in the specification in lines 11 to 20 of page 1 and lines 1 to 3 of page 2. However, the invention does not claim treatment of existing gastric ulcers or the reoccurrence of gastric ulcers but the prevention of the gastric ulcers prior to the occurrence of a gastric ulcer condition as indicated in lines 24 to 26 of page 2 of the application as well as in the rest of the specification. In other words, the claims do not and cannot encompass the use of such active principals for treating existing ulcers in an animal having an ulcer disease condition or for preventing the occurrence of ulcers in an animal which has already suffered from ulcers.

The WO '213 reference merely deals with the treatment of peptic ulcer disease and has absolutely nothing to do with prevention as can be seen from lines 5 and 6 of page 7 of the reference. With respect to the FDA Register relating to omeprazole, this discloses oral use of omeprazole for the treatment of gastric ulcers in horses and foals and for the prevention of a reoccurrence of gastric ulcers in such animals. As clearly explained above, prevention of reoccurrence of gastric ulcers is completely different from the prevention of gastric ulcers by

animals which have never suffered from gastric ulcers. Neither of these two references deal whatsoever with the prevention of gastric ulcers prior to the treatment thereof.

The Papich reference merely summarizes knowledge of the use of omeprazole in the treatment of ulcers. At first glance, Papich states in the introductory part, that many anti-ulcer drugs are prescribed to small animals simply for the prevention of ulcers rather than the treatment thereof because the patient may be disposed to develop gastric intestinal ulcers owing to concurrent disease or drug therapy. Therefore, the "ulcer therapy" referred to in this article includes gastric and intestinal ulcers, ulcer prevention, gastroduodenitis and oesophagitis. It should be noted that Papich deals only with small animals and nothing such as horses.

The prevention of ulcers in small animals is referred to only in the case where the animal is predisposed to develop gastro intestinal ulcers due to concurrent diseases or drug therapy. Such ulcer inducing drug therapies are then developed and there are therapies with anti-inflammatory drugs (NSAIDs) and glucocorticoids as the main example. Also note the developments on page 498.

Omeprazole is said to be of interest in ulcer therapy in small animals if one reverts to the chapter beginning at pages 502 to 504. Omeprazole is said to be of interest for treating gastric ulcers in the last paragraph of page 503 and it is also stated in the same paragraph "for therapy of recurrent ulcers or of ulcers that are resistant to other drugs whereby omeprazole has a clear advantage."

The experimental portion of Papich refers to dogs where ulcers are experimentally induced or in free cats, the beneficial effects were questionable. There is no guidance in Papich that omeprazole may be useful in the prevention of gastric ulcers. It is even less obvious that it would be useful for the prevention of gastric ulcers in small animals which are not simultaneously treated with ulcer inducing drugs. There is absolutely no teaching whatsoever of the use for preventing ulcers in horses. Moreover, on page 505, Papich states that there is still controversies in ulcer therapy and Papich is uncertain as to which therapy is the best. Dogs and cats have negligible basal acid secretion and it is not known whether it is necessary to suppress stomach acidity which is the way omeprazole is known to act. In the summary on page 508, it is stated that perhaps, older drugs to treat ulcers such as antacids are just as effective as a newer

drug. Therefore, Papich in no way teaches Applicant's invention.

The Melnichouk et al reference relates to an experiment where fasting pigs were submitted to a 7 day treatment with 30 mg of lansoprazole. Fasting is known to induce gastric ulcers in pigs but the tests failed to show any significant difference between the treated pigs and the controls. Therefore, the Melnichouk et al reference fails to disclose the prevention of ulcers by administering the product to pigs having never suffered from ulcer conditions. To the contrary, the results which are disclosed in Applicant's invention show that there is a clear advantage in preventing gastric ulcers in animals including in animals which are not treated by ulcer inducing drugs. The Melnichouk et al reference would lead one skilled in the art away from Applicant's invention as the tests failed to show any significant difference between the treated and untreated pigs and it clearly shows that the prevention of ulcers by such administration cannot be predicted. Therefore, the references cited by the Examiner in no way teach Applicant's invention and withdrawal of this ground of rejection is requested.

In view of the amendments to the claims and the above remarks, it is believed that the claims clearly point out

Applicant's patentable contribution and favorable reconsideration  
of the application is requested.

Respectfully submitted,  
Bierman, Muserlian and Lucas

A handwritten signature in dark ink, appearing to read 'Charles A. Muserlian', with a long horizontal flourish extending to the right.

---

Charles A. Muserlian, 19,683  
Attorney for Applicant  
Tel.# (212) 661-8000

CAM:ds

**MARKED UP VERSION OF CLAIMS SHOWING CHANGES MADE**

**Claim 1** (amended) A method for the prevention of gastric ulcers in a [mammal] horse prior to the occurrence of gastric ulcers in a horse comprising administering to a horse in need thereof an effective amount of a proton pump inhibitor to the mammal to prevent gastric ulcers.

**Claim 10** (amended) The method of claim 1, wherein the administering is [periodic] daily.

**Claim 12** (amended) The method of claim 1, wherein the administering is at least during an entire period when the mammal is or is suspected to be under conditions which [may be] are stressful or which may increase the risk of formation of ulcers.

**Claim 16** (amended) The method of claim 1, wherein the proton pump inhibitor is in the form of a formulation for controlled release [and lasting delivery].